Thirty-Minute Application of the S-Caine Peel Prior to Nonablative Laser Treatment

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BACKGROUND. **Advancements in nonablative laser technology necessitate concurrent developments in topical anesthesia, as patients have reported varying degrees of discomfort during these procedures. Although topical anesthetics have proven efficacious, they possess inherent limitations related to ease of use.**

OBJECTIVE. **To evaluate the efficacy of the S-Caine Peel (ZARS Inc., Salt Lake City, UT), a novel topical anesthetic that dries to form a flexible membrane, for induction of anesthesia after only a 30-minute application period.**

METHOD. **Twenty patients received concurrent 30-minute applications of both the S-Caine Peel and a placebo cream randomized to the right and left cheeks in a double-blinded manner. After one pass of the 1450-nm diode laser (Smoothbeam, Candela Corp., Wayland, MA), patients' pain levels were recorded on a visual analog scale (VAS). Both the investigator and an independent observer rated perceived discomfort and immediate skin reaction based on a numerical scale.**

RESULTS. **Differences in VAS scores between active sites (average rating of 15 mm) and placebo sites (average rating of 47 mm) were statistically significant ($P<0.001$). A painless procedure was noted at 50% and 65% of active sites by the independent observer and investigator, respectively. This was statistically different ($P<0.001$) from the independent observer and investigator perception of pain-free procedure at the placebo site, 0% and 5%, respectively.**

CONCLUSION. **The S-Caine Peel provided effective and safe dermal anesthesia after only a 30-minute application period for nonablative laser treatment with the 1450-nm diode laser. The unique vehicle readily delivers anesthetic to contoured regions of the body and eliminates the need for occlusion.**

ZARS INC. SUPPORTED THIS STUDY.

TRADITIONAL ABLATIVE laser systems, although undoubtedly effective for the treatment of moderate photoaging and acne scarring, come with distinct disadvantages of prolonged healing times, risk of pigmentary dyschromias, and potential procedural complications secondary to anesthesia.[1] Recently, nonablative laser technology has gained tremendous popularity among physicians and patients alike. These lasers run the gamut from 585- to 1540-nm wavelengths, as well as the intense pulsed light source. The longer wavelength lasers, especially the 1320-nm Nd:YAG laser and the 1450-nm diode laser, are selectively absorbed by dermal water and, theoretically, are the lasers of choice for selective denaturation and shrinkage of collagen.[2] The 1320-nm Nd:YAG laser has been shown to increase new collagen formation and offers subjective improvement in skin quality.[3] Likewise, the 1450-nm diode laser has been shown to improve rhytides, both of the face and the neck.[4,5] Furthermore, this laser has demonstrated efficacy in the treatment of active acne lesions[6] and atrophic acne scars.[7]

In order to ensure limitation of high temperatures to within the dermis, some form of epidermal cooling is employed. This protects the epidermis from heat-induced damage and lowers the pain stimulus intensity. However, cooling does not render the procedure painless. Improvements in topical anesthesia are prudent with increased use of nonablative laser technology. A rapid onset of action and minimal to no side effects are desirable characteristics of effective topicals. Certain topical anesthetics, including EMLA and ELA-Max, possess unique vehicles aimed at overcoming poor epidermal penetration, an inherent characteristic of topical creams.[8–10] Both creams have been studied in association with laser use only after a 60-minute application under occlusion.[10] The lengthy application period and the need for occlusion are less than ideal.

The S-Caine Peel is a 1:1 eutectic mixture of lidocaine base and tetracaine base in a novel cream vehicle that dries to form a flexible membrane. No additional occlusion is needed, as the flexible

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membrane provides inherent occlusion and can be peeled off immediately before the laser procedure, offering ease of use as compared with predecessor topicals. Speculation has arisen about the hydrating effects of topical anesthetics, especially when used with midinfrared lasers that target water.[11] This study did not investigate the hydrating properties of the S-Caine Peel, but they are assumed to be no different than other topical anesthetics.

Recent studies have demonstrated the efficacy of the S-Caine Peel before various laser procedures. The S-Caine Peel was shown in a double-blind randomized study of 30 patients to be more effective than EMLA with occlusion when applied 30 minutes before full-face single-pass CO_2 laser resurfacing.[12] Before pulsed dye laser (PDL) treatment, the peel was comparably efficacious with three different application times (20, 30, and 60 minutes).[13] This study is the first to investigate the efficacy of the S-Caine Peel after a 30-minute application time for induction of anesthesia before nonablative treatment with the 1450-nm diode laser.

Methods

Twenty healthy adult volunteers (19 females and 1 male) with a mean age of 49 were enrolled in this double-blind institutional review board–approved study. Subjects were excluded if they had a known sensitivity to any of the components of the test cream, if they had damaged or broken skin at the treatment site, or if they were pregnant or breastfeeding. Both the active and placebo peel, identical in texture and appearance, were randomized to the patients' right and left cheeks. After a 30-minute application time, the peel was removed, and immediate evaluation (numerical scale) of erythema, edema, and blanching was performed. Starting with the right cheek of each patient, one nonablative pass with the 1450-nm diode laser (Smoothbeam; Candela Corp., Wayland, MA) was executed with these settings: 10 to 14 J/cm^2, 4-mm spot, 250-ms pulse duration, with a dynamic cooling device (DCD) of 50 ms.

After a 5 to 20 pulse limit, the patient assessed the amount of perceived pain on a visual analog scale (0 to 100 mm, with 0 representing no pain and 100 representing the most pain imaginable). Both the physician investigator and an independent observer subsequently evaluated perceived pain on a numerical scale (0 to 3: rated as no pain, slight pain, moderate pain, or severe pain, respectively). The overall ability of each cream to produce adequate anesthesia was recorded by both objective observers and the patient.

Statistical Analysis

The patients' recorded visual analog results were compared between treatment sides using a repeated-measures analysis of variance. The Wilcoxon signed rank test was used to evaluate the level of observed pain by both the investigator and the independent observer. The McNemar chi-square test was performed to assess for level of pain relief at each treatment site.

Results

Comparison of VAS scores (Figure 1) showed that active sites averaged a rating of 15 mm and that placebo sites averaged 47 mm on the scale ($P<0.001$). Patients stating that they had adequate pain relief and also stating they would use that form of anesthesia again were at 90% of the active sites and 15% of the placebo sites ($P<0.001$). Adequate anesthesia was noted by the investigator for 95% of active sites compared with 20% of placebo sites ($P<0.001$) (Figure 2). Investigator and independent observer perceptions of a pain-free procedure were observed at 50% and 65% of the active sites and 0% and 5% of placebo sites (Figure 3). Side effects were limited to mild erythema at the active sites ($P<0.001$), with one patient developing transient moderate erythema.

Discussion

Anecdotally, the longer wavelength lasers, namely the 1320-nm Nd:YAG and the 1450-nm diode laser, tend to elicit a more painful response than other nonablative laser systems. Patients did report significantly more pain on the placebo-applied side of their face, and 90% of patients felt that the peel provided adequate anesthesia. There have been several published studies evaluating lasers for nonablative dermal remodeling, but only a handful have included a

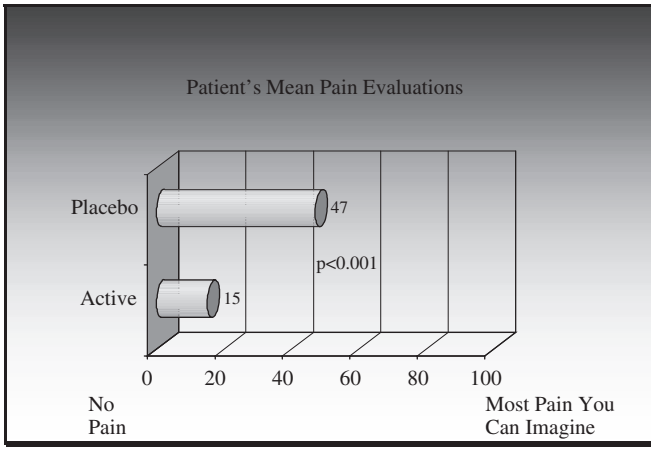

Figure 1. Patients' mean pain evaluations.

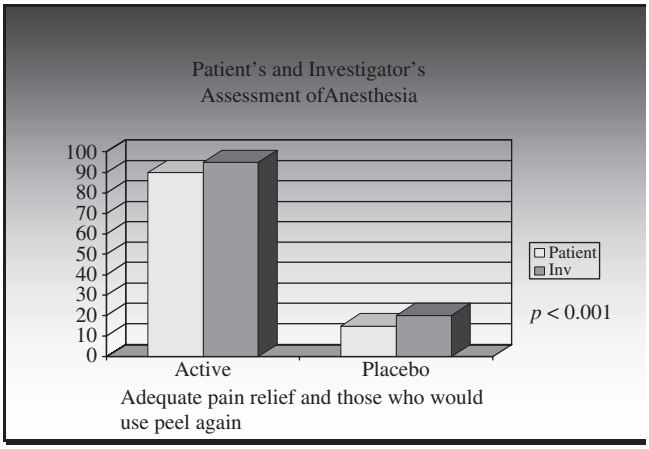

Figure 2. Patients' and investigator's assessment of anesthesia.

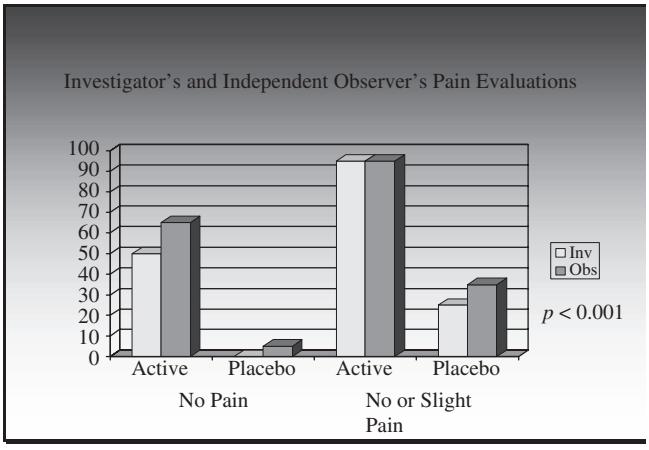

Figure 3. Investigator's and independent observer's pain evaluations.

measurement of patient pain. In a study of 10 patients evaluating photoaging response to treatment with the 1320-nm Nd:YAG laser, pain was graded as severe by 3 of 10 patients, significant by 2 of 10 patients, and mild to significant by 3 of 10 patients.[2] In this study, cryogen cooling with the dynamic cryogen cooling device was used; however, no topical anesthetic was employed. In a phase I study of 10 patients evaluating the use of the 1450-nm diode laser for cutaneous remodeling, a heating cycle of 150 to 500 ms was applied over two to six treatment cycles. Patients did not rate their pain based on an ordinal scale but described their pain as minimal with a tendency toward increasing discomfort when longer heating times were employed.[14]

With limited literature on reported pain with various laser systems, it can only be speculated why certain laser systems engender a more painful sensation than others. Evaluation of the efficacy of any topical anesthetic after laser induced stimulus is ideal, as pain evoked is highly reproducible, well-controlled, and measurable. It is also a more clear measurement of pain caused by nociceptor activation without interference from mechanosensitive receptors.[15,16] The long wavelength lasers target water in the papillary dermis, where a majority of facial sensory nerve fibers terminate.[16] Cutaneous sensations from laser injury seem to be conducted by both C-fibers and Aδ-fibers and are perceived as snapping and pinprick sensations followed by a sensation of heat.[16] Local anesthetics block the transmission of action potentials in thin unmyelinated fibers, which transmit the sensation of warmth, before blocking action potentials of thicker myelinated fibers, which transfer a pinprick sensation. Following this principle, after the application of local anesthesia, the sensation of warmth should disappear before the pinprick sensation. Because the opposite occurs, Arendt-Nielson speculated that warmth receptors are located deeper in the dermis.[15] Perhaps longer wavelength lasers act not only on superficial nociceptors in the papillary dermis that produce the pinprick sensation but also provoke these deeper heat receptors leading to an increased perception of pain. In studies using the CO_2 laser to study cutaneous pain thresholds, increased pulse duration was found to lower pain thresholds. Furthermore, higher stimulus intensities had a direct relationship to perceived pain, and beam size had an inverse relationship to the amount of energy needed to reach pain threshold.[17] The parameters of the longer wavelength lasers used for nonablative dermal remodeling may contribute to the increased pain perceived by the patient.

Adequate dermal anesthesia is a requisite while using these longer wavelength lasers. The S-Caine Peel, an eutectic mixture of lidocaine and tetracaine, provides a unique cream base that dries to form a flexible membrane that can be peeled off. The cream offers demonstrable ease of use, quick onset of action, and minimal to no local adverse effects. Our studies mirror findings of previous studies that the peel is highly efficacious at inducing dermal anesthesia after a 30-minute application period. Furthermore, longer wavelength subsurfacing can now be added to the expanding list of laser procedures in which the S-Caine Peel has proven valuable.

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